Claims 2-21 are definite and recite the claimed subject matter with particularity

The Examiner has rejected Claims 2-21 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. For example, the Examiner rejected Claim 2 because the recitation of "a pharmaceutically effective amount of nerve growth factor" failed to indicate the conditions for which the amount of growth factor would be effective. "[D]uring examination proceeding, claims are given their broadest reasonable interpretation consistent with the specification." In re Hyatt, 211 F.3d 1367. 1372 (Fed. Cir. 2000). The above-referenced application is directed to stabilized preparations of nerve growth factor (NGF), rather than preparations of NGF for use in treating a particular disease state. Accordingly, the rejected claim language would encompass any concentration of NGF that would be pharmaceutically effect to treat any condition. This scope of the recited subject matter is in keeping with the disclosure of the specification, which provides teachings for the preparation of a stabilized NGF formulation. This is the proper scope of the claim and thus the metes and bounds of the amount of NGF encompassed by the claims is defined with sufficient definiteness and particularly to satisfy the requirements of 35 U.S.C. § 112, second paragraph. Accordingly, Applicants submit that this rejection should be withdrawn.

The Examiner has alleged that Claim 13 is indefinite because it recites "at least about 0.1 mg/ml" of NGF. One purpose of 35 U.S.C. § 112, second paragraph is to provide the public with clear boundaries regarding the scope of the subject matter encompassed by a patent claim. Applicants suggest that the rejected term should be given its plain meaning to determine the metes and bounds of the claim. Infringement of Claim 13 could easily be determined using a standard NGF quantitation assay, such as the PC-12 cell survival bioassay, taught in Example II. Claim 13 is definite because one of ordinary skill in the art could easily determine whether or not they were infringing the subject matter of Claim 13. Accordingly, the rejection of this claim should be withdrawn.

Claims 10, 13-15, and 16 were rejected as allegedly lacking antecedent basis in Claim 2. Each of these claims have been amended to more accurately recite the claimed subject matter.

Claims 6, 15, and 16 have been rejected because each recites an undefined acronym. Claim 2 has been amended to recite the acronym, thus providing antecedent basis for this term in Claims 6, 15, and 16.

Claim 21 has been amended to clarify that the NGF recited therein is purified from NGF cells.

Applicants believe that all grounds for rejection of Claims 2-21 have been overcome and request that the rejection of Claims 2-21 under 35 U.S.C. § 112, second paragraph be withdrawn.

The pending claims are novel over the Calbiochem 1994/1995 product catalog.

Claims 2-21 stand rejected under 35 U.S.C. § 102(b) as being allegedly being anticipated by the 1994/1994 Calbiochem product catalog. A rejection under 35 U.S.C. § 102 requires that an anticipating reference teach each and every limitation of the pending claims. Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631 (Fed. Cir. 1987); M.P.E.P. § 2131. Applicants respectfully traverse the rejection of the pending claims under 35 U.S.C. 102 in that the cited prior art reference does not teach all of the limitations of the pending claims.

Claims 2 and 18 are the independent claims pending in the above-referenced application. Each recites a pharmaceutical composition comprising NGF and a pharmaceutically acceptable acetate-containing buffer. The term "pharmaceutically acceptable" defines a particular quality level of the buffer such that a composition containing said buffer would be suitable for use as a pharmaceutical agent. As the products offered for sale in the Calbiochem product catalog are presumed to be used for research purposes only, the Examiner has failed to demonstrate that the buffer used for the products listed are pharmaceutically acceptable. Accordingly, this reference fails to teach each and every limitation of the claimed invention. Therefore, Applicants respectfully request withdrawal of this rejection.

Claims 2, 4, 5, and 18 are novel over Apfel.

The Examiner has rejected Claims 2, 4, 5, and 18 stand rejected under 35 U.S.C. § 102(b) as being allegedly being anticipated by Apfel, et al., Annals of Neurology, 29: 87-90 (1991). Applicants respectfully traverse the rejection of Claims 2, 4, 5, and 18 under 35 U.S.C. 102 in that the cited prior art reference does not teach all of the limitations of the pending claims.

As discussed above, Claims 2 and 18 are the independent claims pending in the above-referenced application. Each recites a composition comprising NGF and a pharmaceutically acceptable acetate-containing buffer. The term "pharmaceutically acceptable" defines a

particular quality level of the buffer such that a composition containing said buffer would be suitable for use as a pharmaceutical. Because Apfel administered NGF to mice, there is no reason to assume that the quality of the acetate-containing buffer allegedly described therein was of a pharmaceutically acceptable quality. In fact, given the experimental work discussed in Apfel, it is presumed that the compositions discussed therein are suitable for research purposes only. Accordingly, the Examiner has failed to demonstrate that the buffer used for the products listed are pharmaceutically acceptable. Thus, this reference fails to teach each and every limitation of the claimed invention and the pending rejection of Claims 2, 4, 5, and 18 should be withdrawal.

Claims 2-6, 11-14, 17, 18, and 20 are novel over Della Valle (U.S. Patent No. 5,210, 185) because Della Valle does not teach the purification of NGF.

Claims 2-6, 11-14, 17, 18, and 20 are novel over Della Valle (U.S. Patent No. 5,210, 185) because Della Valle does not teach a pharmaceutically composition comprising a pharmaceutically acceptable acetate-containing buffer. The claimed subject matter recites a pharmaceutical composition comprising, *intra alia*, a pharmaceutically acceptable acetate-containing buffer. As discussed above, such a buffer would have certain art recognized quality characteristics that would make the buffer suitable for use as a pharmaceutical agent. Della Valle specifically discusses pharmaceutical compositions on column 6, line 65 to column 9, line 26. Nowhere in this discussion does Della Valle discuss the use of an acetate-containing buffer. Because Della Valle does not teach a pharmaceutically composition comprising a pharmaceutically acceptable acetate-containing buffer, this reference does not anticipate Claims 2-6, 11-14, 17, 18, and 20. Accordingly, this rejection should be withdrawn.

Claims 2, 3, 5, 6, 11-14, and 18 are novel over Knepp et al. (WO 95/058845).

Claims 2, 3, 5, 6, 11-14, and 18 are novel over Knepp (WO 95/058845) because Knepp does not disclose a pharmaceutically composition comprising a pharmaceutically acceptable acetate-containing buffer. The claimed subject matter recites a pharmaceutical composition comprising, *intra alia*, a pharmaceutically acceptable acetate-containing buffer. As discussed above, such a buffer would have certain art recognized quality characteristics that would make the buffer suitable for use as a pharmaceutical agent. Knepp discusses biologically acceptable

compositions rather than pharmaceutical compositions. Because Knepp does not teach a pharmaceutically composition comprising a pharmaceutically acceptable acetate-containing buffer, this reference does not anticipate Claims 2, 3, 5, 6, 11-14, and 18. Accordingly, this rejection should be withdrawn.

The pending claims are not obvious in over Della Valle in view of Remington.

The Examiner has rejected Claims 2-20 as being obvious over Della Valle in view of Remington. To make out a *prima* facie case of obviousness under 35 U.S.C. § 103 requires that, *inter alia*, the cited art references teach or suggest all the limitation of the pending claims. Applicants submit that no *prima facie* case of obviousness has been articulated because this requirement has not been met by the cited art.

As discussed above, Della Valle does not teach or suggest the use of a pharmaceutically acceptable acetate-containing buffer. That a acetate-containing buffer was used during purification in Della Valle does not mean that one of ordinary skill in the art would have used such a buffer to make a pharmaceutical composition containing NGF using an acetate-containing buffer. Remington does not cure this defect in Della Valle as it does teach pharmaceutical compositions containing NGF. Because Della Valle taken alone or in combination with Remington fails to teach the claimed invention, these reference do not render the subject matter of the pending claims obvious. Thus, this rejection should be withdrawn.

Claims 18 and 21 are not obvious in over Della Valle in view of Heinrich (U.S. Patent No. 5,082,774).

Claims 18 and 21 stand rejected as allegedly being obvious over Della Valle in view of Heinrich. Applicants submit that no *prima facie* case of obviousness has been articulated with the citation of these references because the references, either alone or in combination, fail to teach the claimed invention.

Della Valle does not teach or suggest the use of a pharmaceutically acceptable acetate-containing buffer. Heinrich fails to cure this defect of Della Valle as it too fails to teach a pharmaceutically acceptable acetate-containing buffer. Because Della Valle taken alone or in combination with Heinrich fails to teach the claimed invention, these reference do not render the subject matter of the pending claims obvious. Thus, this rejection should be withdrawn.

Claims 2-14 and 17-20 are not obvious in over Knepp, in view of Della Valle, Heinrich, Remington, Schmelzer, and O'Connor.

Claims 2-14 and 17-21 stand rejected as allegedly being obvious over Knepp, in view of Della Valle, Heinrich, Remington, Schmelzer, and O'Connor. Applicants submit that no *prima facie* case of obviousness has been articulated with the citation of these references because the references, either alone or in combination, fail to teach the claimed invention.

Knepp does not teach a pharmaceutical composition comprising a pharmaceutically acceptable acetate-containing buffer. In fact, none of the cited reference teach a pharmaceutical composition comprising NGF and a pharmaceutically acceptable acetate-containing buffer. Because neither Knepp alone or in combination with any of the secondary references cited teaches the claimed invention, Claims 2-14 and 17-21 are not obvious in view of the cited art.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the claims are patentable and in condition for allowance. Accordingly, withdrawal of the rejections and allowance of the claims is earnestly solicited. Applicants believe that all points raised in the Office Action have been addressed herein. Nevertheless, if minor matters remain, the Examiner is invited to contact the undersigned at the number below.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: APR 2002

By:

James J. Mullen III, Ph.D.
Registration No. 44,957
Attorney of Record
620 Newport Center Drive
Sixteenth Floor
Newport Beach, CA 92660
(619) 235-8550

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Please amend Claims 2, 10, 13, 14, 15, 16, and 21 as follows:

2. (Amended) A pharmaceutical composition comprising a pharmaceutically effective amount of nerve growth factor (NGF) and a pharmaceutically acceptable acetate-containing buffer.

10. (Amended) The composition of claim 2, further comprising a ~~wherein the~~ benzyl alcohol concentration ~~is form~~ from 0.1 to 2.0%

13. (Amended) The composition according to claim 2, wherein the nerve growth factor has a concentration of at least about 0.1 mg/ml and said acetate-containing buffer comprises an acetate ion ~~has~~ having a concentration of 10 mM to 50 mM.

14. (Amended) The composition according to claim 2, wherein said nerve growth factor has a concentration of 0.1 to about 2.0 mg/ml and said acetate-containing buffer comprises an acetate ion ~~has~~ having a concentration of 10 mM to 50 mM.

15. (Amended) The composition of claim 2, wherein the NGF concentration is 0.1 mg/ml, the acetate-containing buffer is 20 mM sodium acetate, ~~the sodium acetate concentration is 20 mM,~~ and wherein the composition further comprises a ~~the pH is 5.5, the~~ sodium chloride concentration ~~is~~ of 136 mM, ~~and~~ a benzyl alcohol concentration ~~is~~ of 0.9% (v/v), and wherein the composition is about pH 5.5.

16. (Amended) The composition of claim 2, wherein the NGF concentration is 2.0 mg/ml, the acetate-containing buffer is 10 mM sodium acetate, ~~the sodium acetate concentration is 10 mM, the pH is 5.5, and the~~ and wherein the composition further comprises a sodium chloride concentration ~~is~~ of 142 mM, and wherein the composition is about pH 5.5.

21. (Amended) The composition of claim 18, wherein the nerve growth factor is secreted and purified from Chinese hamster ovary cells.